Update in Cardiology
What’s Hot in 2017?

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Disclaimer

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Update in Cardiology-What’s Hot in 2017?

• Atrial fibrillation
• Lipids
• Heart Failure
• **Atrial fibrillation – Why is it important?**
  – The most common rhythm disturbance we treat
  – An arrhythmia of an aging population
    • About 6% of people over 65 have afib
    • Those >70 – about 20% will have afib as either a temporary or permanent rhythm disturbance
  – Very common cause of stroke
    • Afib increases your risk for stroke by 5 times
    • About 15-20% of ischemic strokes are caused by afib
• **Atrial fibrillation – Treatment**

  – Rate control vs. rhythm control?

  • Depends on the patient
    – Beta-blockers, calcium channel blockers
    – Antiarrhythmics +/- cardioversion
    – Ablation therapy
Atrial fibrillation – Anticoagulation

Underutilized!
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Influence of Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation

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- 655,000 patients from NCDR database with non-valvular afib
- Patients with prior valve surgery or contraindication to OAC excluded
- CHA₂DS₂-VASc > 1

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• Results

— Overall rate of OAC use was about 52%
— Introduction of DOAC’s increased that rate to only about 60%
— Considerable practice variation in use of OAC therapy
• Atrial fibrillation – Anticoagulation

What do the guidelines say?

– Evolved over time to become more aggressive

• ACC/AHA/HRS Guidelines from 2014
  – CHA₂DS₂-VASc = 0 Reasonable to omit anti-thrombotic Rx
  – CHA₂DS₂-VASc = 1 No treatment or oral AC or ASA
  – CHA₂DS₂-VASc ≥ 2 Oral AC
    » Mod-severe CKD – reduced doses of DOAC’s
    » ESRD/HD – warfarin
  – These are all either class IIA or IIB recommendations meaning Benefit >> Risk or Benefit ≥ Risk with LOE either B or C meaning limited or very limited populations studied.
Atrial fibrillation – Anticoagulation

- Does the type of Afib make a difference?
  - Paroxysmal - at least two separate episodes of AF that terminate spontaneously in less than 7 days, usually within 24 hours.
  - Persistent – does not convert to SR without Rx within 7 days
  - Permanent/chronic

- Risk of stroke is THE SAME for both paroxysmal and persistent/permanent AF
DOAC’s – Some considerations

• Cost for 30-day supply*
  – Warfarin $11
  – Edoxaban $326
  – Rivaroxaban $371
  – Dabigatran $383
  – Apixaban $401

* https://www.goodrx.com/anticoagulants
• **Atrial fibrillation – What’s the “Take Home”?**
  - Take a history
    - Significant bleeding history or frequent falls
  - Rate vs. rhythm control
    - Involve your favorite cardiologist
  - Type of afib? – It doesn’t matter!
    - Risk of stroke is **THE SAME** regardless of type
  - Use the CHA\textsubscript{2}DS\textsubscript{2}-VASc Score and document
  - Document why you’re **NOT** anticoagulating a patient
  - Stop using the term “new onset afib”
Atrial fibrillation – What’s the “Take Home”?  
– What about ablation therapy?
* Reserved for those patients with symptomatic AF who have failed multiple attempts at trying to achieve SR
* About a 23% initial failure rate at 6-9 months
* Maybe a placebo effect?
* Doesn’t get rid of need for long-term anticoagulation
* Done despite no proven mortality benefit or stroke risk reduction
• Lipids – What’s Hot?

PCSK-9 Inhibitors
• Lipids – PCSK9
  – Proprotein convertase subtilisin/kexin type 9 (PCSK9)
    • Binds to LDL receptors in the liver and breaks down the receptor so that it can no longer remove LDL from the blood
    • Overexpressed in familial hypercholesterolemia
• **Lipids – PCSK9 Inhibitors**
  
  – Monoclonal antibodies that bind to and inactivate PCSK9

• **Evolocumab (Repatha®)**
  
  – 140mg SQ Q2Weeks for primary hyperlipidemia with CVD or heterozygous FH
  
  – 420mg Qmonth or Q2Weeks for homozygous FH

• **Alirocumab (Praluent®)**
  
  – 75mg Q2Weeks
• Lipids – PCSK9 Inhibitors – Clinical trials
  – OSLER-1 and 2 showed safety and efficacy
  • Either agent when combined with a statin lower cholesterol better than with statin therapy alone (60% better).
  – More than 40 trials now in various stages of progress to assess effects on CV morbidity and mortality
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- **Lipids – PCSK9 Inhibitors – Clinical trials**
  - **FOURIER Trial**
    - 27,564 patients with ASCVD and LDL $\geq 70$mg/dl who were on max tolerated statins received Evolocumab or placebo
    - **Primary efficacy endpoint**
      - Composite of CV death, MI, stroke, hospitalization for UAP, or coronary revascularization
    - **Secondary efficacy endpoint**
      - Composite of CV death, MI, or stroke
    - **Median follow-up 2.2 years**

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• Lipids – PCSK9 Inhibitors
  – FOURIER Trial – RESULTS
  • Mean percentage reduction in LDL was 59% (92 mg/dl $\rightarrow$ 30 mg/dl)
  • Significantly reduced the risk of the primary endpoint (9.8% v 11.3%, $p<0.001$) and the secondary endpoint (5.9% v 7.4%, $p<0.001$)
**Lipids – PCSK9 Inhibitors**

- **FOURIER Trial – CONCLUSIONS**
  - Evolocumab plus statin
    - Lowered LDL cholesterol to a median of 30 mg/dl
    - Reduced risk of cardiovascular events
      - reduced risk of stroke by 0.4%
      - reduced risk of MI by 1.2%
      - reduced risk of coronary revascularization by 1.5%
    - Patients with ASCVD benefit from lowering LDL cholesterol levels below current targets
    - But, no reduction in CV or all cause death rates
• **Lipids – PCSK9 Inhibitors**
  – **COST**
    • Evolocumab for one year about $14,350
    • NNT in FOURIER trial was 74
      – Cost would be about $2.1 million to prevent one event over two years.

Cost will need to come down
• Lipids – PCSK9 Inhibitors

– INDICATIONS

• Approved as adjuncts to diet and maximally tolerated statin therapy for patients with familial hypercholesterolemia (FH), and those with clinical atherosclerotic cardiovascular disease (ASCVD), requiring a greater reduction in LDL-C levels.

• Evolocumab approved for patients with:
  – Clinical ASCVD, HeFH, HoFH

• Alirocumab approved for patients with:
  – Clinical ASCVD, HeFH
Heart Failure
Neprilysin Inhibitors
• **What’s Neprilysin?**
  
  – Neutral endopeptidase produced by many tissues but markedly so by the kidney and lung
  – Cleaves peptides and it inactivates several peptide hormones
    • Glucagon
    • Enkephalins – endogenous opioids in the CNS
    • Oxytocin – vasopressin-like properties
    • Angiotensin II - vasoconstrictor
    • Endothelin – vasoconstrictor
    • Bradykinin
    • Atrial natriuretic factor – powerful vasodilator and promotes natriuresis (opposite effect of aldosterone)
• What do Neprilysin inhibitors do?
  – Interrupt portions of the RAAS and Natriuretic Peptide System to:
    • Promote vasodilatation, natriuresis, and diuresis
    • Decrease Sympathetic tone
    • Decrease fibrosis and myocyte hypertrophy
    • Decrease aldosterone secretion
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• Neprilysin Inhibitor – PARADIGM HF Trial

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

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PARADIGM-HF Conclusions

- LCZ696 more effective than ACEI in reducing death from cardiovascular causes or hospitalization for HF
- LCZ696 superior to enalapril in reducing all cause mortality and symptoms/physical limitations from HF
- Significance of findings apparent across all subgroups
- Strong evidence that ARNI’s are superior to inhibition of the RAAS alone
• **PARADIGM-HF Criticisms**
  
  – Max recommended HF dose for valsartan used while max recommended dose of enalapril not used (10mg BID vs 20mg BID)*
  
  – Too stringent inclusion criteria
  
  – Study terminated early
  
  – Expense – What’s the incremental benefit when combined with other therapies?
    
    • Sacubitril/valsartan - $ 12.50/day or about $4,500/year
    
    • Enalapril - $ 1.20/day or about $440/year
  

* Average daily dose of enalapril in CONSENSUS was 18.4 mg daily
Class I-B recommendation

“In patients with chronic symptomatic NYHA Class II or III HFReF who tolerate an ACEI or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.”
MOC Quiz Question

An 82 yo patient with paroxysmal atrial fibrillation that is symptomatic with a sensation of palpitations when in rapid ventricular response and a CHA₂DS₂-VASc score of 2; no history of falls or bleeding problems with normal renal function should:

A. Be anticoagulated with warfarin or a DOAC.
B. Receive a beta-blocker or non-dihydropyridine CCB.
C. A and B.
D. Receive an antiarrhythmic agent plus an atrial defibrillator.
E. Undergo afib ablation.
Concluding Thoughts
“What this patient needs is a doctor.”
-Eugene A. Stead, Jr., MD
1908-2005
Anticoagulation - What you need to know

Atrial fibrillation

• **CHA$_2$DS$_2$-VASc Score**
  - Stroke risk assessment tool
    - C – CHF 1 point
    - H – Hypertension 1 point
    - A$_2$ – Age ≥ 75/Age 65-74 2/1 point
    - D – Diabetes mellitus 1 point
    - S$_2$ – Prior stroke or TIA/Sex (female) 2/1 point
    - VASc – Vascular disease 1 point
### Exclusion Criteria

*If the answer to ANY item below is met, then the patient should NOT receive sacubitril/valsartan*

- □ Current acute decompensated heart failure (refers to initial therapy only)
- □ Hypersensitivity to any component of sacubitril/valsartan
- □ History of angioedema related to an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB)
- □ History of intolerable side effects to an ARB
- □ Concomitant treatment with aliskiren in patients with diabetes
- □ Need for continued therapy with an ACEI, ARB alone, or direct renin inhibitor (aliskiren)
- □ Symptomatic hypotension
- □ Systolic blood pressure (SBP) < 100 mm Hg
- □ Severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/min/1.73m²) (Refer to Issues for Consideration)
- □ Severe hepatic impairment (Child-Pugh C) (Refer to Issues for Consideration)
- □ Serum potassium > 5.2 mEq/L
- □ History of non-adherence to guideline directed medical therapy for heart failure despite counseling (< 80% medication possession ratio)
- □ Pregnancy (i.e., known pregnancy or positive pregnancy test) (Refer to Inclusion Criteria and Monitoring)

### Inclusion Criteria

*The answers to all of the following must be fulfilled in order to meet criteria.*

- □ Restricted to VA Cardiology for initial prescription (Refer to Issues for Consideration)
- □ New York Heart Association (NYHA) Class II-IV heart failure symptoms (Refer to Issues for Consideration)
- □ Left ventricular ejection fraction (LVEF) ≤ 35% (Refer to Issues for Consideration)
- □ Most recent (while on therapeutic, or maximally tolerated, doses of evidence-based recommended medications for heart failure, as indicated) B-type natriuretic peptide (BNP) ≥ 150 pg/ml (or N-terminal pro-BNP [NT-pro-BNP] ≥ 600 pg/ml), OR a BNP > 100 pg/ml (or NT-pro-BNP > 400 pg/ml) if the patient had been hospitalized for heart failure in the past 12 months
- □ Receiving a stable dose (i.e., ≥ 4 weeks) of a beta-blocker (after titration to maximally tolerated target dose as recommended by clinical practice guidelines), or documented intolerance or contraindication to a beta-blocker
- □ Receiving a stable dose (i.e., ≥ 4 weeks) of an ACEI or ARB (after titration to maximally tolerated target dose as recommended by clinical practice guidelines, and equivalent to at least enalapril 10 mg per day) Note: if sacubitril/valsartan is prescribed, other ACEI or ARB will need to be discontinued (Refer to Dosage and Administration, and Issues for Consideration)

For women of childbearing potential,

- □ pregnancy should be excluded prior to receiving sacubitril/valsartan and the patient provided contraceptive counseling on potential risk vs. benefit of taking sacubitril/valsartan if patient were to become pregnant (Refer to Monitoring)